REMARKS

Claims 1-43 are pending in the instant application. Applicants have added claim 44, amended claims 1, 2, 9, 11, 12, 13, 21, 29, 41, and 42; and canceled claims 19-20, 22-27, and 36-40 without prejudice or disclaimer to their later reintroduction. Applicants amended claims 11, 13, 41, and 42 to correct informalities, as requested by the Office. The specification provides support for amended claims 1, 2, 9, 12, 21, and 29; and added claim 44, as summarized in the chart below:

Claim	Specification Support
1	Example 2, page 23, lines 25-27.
2	Page 20, lines 13-16.
9	Original claim 9.
12	Original claim 12.
21	Original claim 21; Example 2, page 23, lines 25-27.
29	Page 20, lines 13-16.
44	Original claim 21.

No new matter is added. With the entry of this amendment, claims 1-18, 21, 28-34, and 41-44 are currently pending.

Applicants have amended the title to more clearly reflect the claims of this application.

Claim Objections

The Office objected to claims 11, 13, 21, 40, and 42 because of various informalities. Applicants have amended the claims as follows.: In claim 11, "and" has been replaced with "or." In claim 13, "incorporate" has been replaced with "incorporated. In claim 21, line 6, the

"and" preceding daidzein has been replaced with "or." In claim 42, line 2, "treatment" has been replaced with "treating." Applicants have cancelled claim 40. Applicants have also removed a redundant phrase in claim 41. Thus, with the entry of this amendment, any objections noted in the pending office action must be withdrawn.

Claim Rejections

35 USC § 112

The Office rejected claims 9, 12, 19, 20, 21, and 25 under § 112, second paragraph. The Office states that the phrase "such as" renders claims 9, 19, and 21 indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. The Applicants have cancelled claim 19 and amended claims 9 and 21 to delete the phrase "such as."

The Office rejected claim 12 due to the parenthetical limitation "(0.5g to 2 g)." The Applicants have amended claim 12 to omit this parenthetical.

The Office rejected claims 19 and 20 for lack of any steps involved in the method/process. The Office also rejected claims 19-20 under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process. The Applicants have cancelled claims 19 and 20, thus rendering the rejection moot.

The Office states that claim 25 lacks antecedent basis for the limitation in line 1, "to reduce the risk of vascular disease". Applicants have cancelled claim 25 thus rendering the rejection moot.

With the entry of Amendment and Response, the § 112 rejections noted in the pending Office Action must be withdrawn.

35 USC § 103

The Office rejected claims 1-43 under 35 U.S.C. § 103(a) as unpatentable over Kelly WO 93/23069 ("Kelly '069") in view of Empie et al., U.S. Patent No. 6,261,565 B1 ("Empie") and Kelly 6,340,703 ("Kelly '703"). The Office states that Kelly '069 discloses compositions enriched with phyto-estrogens selected from genistein, daidzein, formononetin and biochanin A for promoting health in cases of cancer, premenstrual syndrome, menopause or hypercholesterolemia. The Office also states that Kelly '069's preferred ratio for genistein and/or biochanin A to daidzein and/or formononetin is 1:2 to 2:1 and that the compositions may be used to lower LDL thus leading to a reduced risk of developing atherosclerosis. Finally, the Office states that Kelly '069 does not specifically disclose using the compositions for treating osteoporosis or cardiovascular disease or vascular diseases or bone fractures.

The Office refers to Empie as disclosing compositions prepared by extracting phytochemicals from soy or red clover, wherein the resulting composition comprises isoflavones consisting predominantly of genistein and/or biochanin A and/or formononetin with a ratio of genistein to daidzein from 100:1 to 1:100. The Office states Empie additionally discloses that isoflavones are known to be useful in treating osteoporosis, vascular effects, and cardiovascular diseases, including heart disease.

The Office also refers to Kelly '703 as disclosing a method of treating osteoporosis by administering to a patient in need thereof a composition containing an effective amount (10:1 to 1:10) of formononetin and daidzein.

The Office concludes that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods and compositions of Kelly '069 for use in treating osteoporosis, vascular disorders or cardiovascular disorders because in view of

Empie's and Kelly's '703 disclosure, one of ordinary skill in the art would reasonably expect the substantially similar isoflavone containing compositions of Kelly to be effective in treating such disorders." The Office also concludes the claims drawn to treating or preventing bone fracture would have been obvious because one of ordinary skill in the art would reasonably expect the treatment of osteoporosis to reduce the likelihood of bone fractures.

The Office also states that it would have been obvious to one of ordinary skill in the art to modify the compositions of Kelly and Empie with additional calcium to help treat patients suffering from osteoporosis and bone fractures. Similarly, the Office states it would have been obvious to one of ordinary skill in the art to choose from a variety of known vitamins such that the overall composition is nutritionally balanced.

Finally, the Office states that "since Kelly '069 and '703 and Empie have established that the therapeutic efficacy of the isoflavones is dependent upon their ratio amounts, it would have been obvious to one of ordinary skill in the art to further modify the methods and compositions of Kelly and Empie such that the isoflavones are present in a ratio that is effective to optimize their therapeutic activity."

Applicants respectfully traverse on a number of bases.

First, solely to expedite prosecution and without disclaimer of the deleted subject matter or prejudice to its later reintroduction in future continuation or divisional applications, Applicants have amended both the composition and method claims to recite "formononetin and one or more isoflavones selected from biochanin, genistein and daidzein" at a ratio of "15:1 to 4:1." In addition, the independent method claim now recites a method based on this same composition for the beneficial alteration or treatment of bone density or for the prevention or treatment of bone fracture. Thus, as set forth in the Summary of the Invention at page 10, the

invention relates to "compositions comprising high proportions of formononetin" relative to the other isoflavones, biochanin, genistein and daidzein.

Second, the Kelly patent, U.S. Patent No. 6,340,703, cannot be applied as prior art against this application because it is not the invention "of another." The disclosure in the Kelly '703 patent relating to formononetin (which is preferably "substantially unaccompanied by other isoflavones") and osteoporosis derives from the invention of Dr. Graham E. Kelly, the sole inventor of the Kelly '703 patent and one of the joint inventors of the present application. The disclosure in the present application relating to a specific range of ratios of formononetin and one or more isoflavones and for the use of that composition for the maintenance of bone density and for the treatment of osteoporosis is also the invention of Dr. Kelly. Applicants hereby submit a declaration by Dr. Kelly attesting to his sole inventorship of the use of formononetin, per se, and in specific ratios, for enhancing bone density, for improving bone resorptions and turnover, and to treat osteoporosis, as well as a declaration by co-applicant, Dr. Alan J. Husband, confirming the same. Thus, the Kelly '703 patent cannot be applied against the present invention.

Neither of the other recited references teaches or suggests "high proportions of formononetin." Indeed, both references expressly teach away from this concept.

Beginning with the Kelly '069 publication, it teaches a composition of any or all four isoflavones. The "Disclosure of Invention" at page 8 recites a supplement "specifically enriched for isoflavones selected from genistein, daidzein, formononetin, and biochanin A." It later states that the ratio of genistein (and/or its derivative biochanin A) to daidzein (and/or its derivative formononetin) is between 1:2 to 2:1. This ratio poses the ranges possible for the two groups of isoflavones, with nothing about high proportions of formononetin.

Later, however, the Kelly '069 specification makes clear that it does not matter whether or not formononetin or its demethylated form, daidzein, is present, as follows:

> It is thought that because the methyl forms (biochanin A and formononetin) ultimately are largely demethylated to their principles, genistein and daidzein, with improved biological efficacy, then it is *unimportant whether the isoflavones are present in the claimed product in methylated or demethylated forms*.

Specification, page 10, paragraph 2 (emphasis added). And still later the specification teaches that "it is prudent that both [isoflavone groups (being genistein and daidzein)] be present in the claimed product in *approximately equal proportions*. *Id.* paragraph 3 (emphasis added). Finally, as the Office acknowledged, the Kelly '069 publication does not disclose treating osteoporosis or bone fractures. Thus, it teaches away from "high proportions of formononetin" and is completely silent on the use of any isoflavone compositions for bone maladies.

Empie, the '565 patent, similarly teaches away from "high proportions of formononetin." Its background section concludes with the express proposition that "a need exists for an improved composition consisting substantially of isoflavones, lignans, saponogenins, saponins, and/or phenolic acids which will produce improved results *over any of these taken alone*." Col. 3, lines 31-34 (emphasis added). Correspondingly, the Detailed Description begins by teaching that "the improved composition is obtained by fractionating a plant source high in isoflavones, lignans, and other phytochemicals…," col. 4, lines 16-18, and than later provides proportions for these mixtures, as follows:

> The resulting composition is expected to comprise in a preferred from [sic]: between 5% and 95% isoflavones, between 0% and 70% lignans, and between 2% and 70% saponins and sapogenins.

Col. 4, lines 44-47.

The paragraph does discuss a ratio of the derivatives of genistein (and/or its precursor biochanin) to derivatives of daidzein (and/or its precursor formononetin) of from 100:1 to 1:100, but that range merely covers the entire spectrum. And none of the isoflavone-based compositions made in Examples 1-4 indicate the amounts of the specific isoflavones. The separate solutions in Example 5 were made merely to test solubility and do not even include one based on formononetin.

Finally, while Example 1 does mention osteoporosis, it does not even indicate whether the isoflavones are responsible for the beneficial results. It concludes that "isoflavones *or lignans* can alleviate menopausal-related symptoms such as hot flashes and osteoporosis…." Col. 7, lines 4-5.

Thus, Empie expressly teaches the value of mixtures of these various phytochemicals, and specifically teaches mixtures of isoflavones. Because both teachings are diametrically opposed to "high proportions of formononetin," Empie teaches away from the claimed invention.

As is well established, the Office cannot set forth a *prima facie* case of obviousness based upon references that teach away from the claimed invention. Manual of Patent Examining Procedure ("MPEP") § 2145 at 2100-161 (Eighth Ed.; 2nd Rev., May 2004); *In re Hedges* 783 F.2d 1038, 1041 (Fed. Cir. 1986). Accordingly, Applicants respectfully request the withdrawal of rejection.

Double Patenting

The Office rejects claims 1, 2, 9, 19-21, 28, and 35 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6, 9, 14, and 15 of U.S. Patent No. 6,340,703. Applicants have cancelled claims 19 and 20. Without acquiescing to the rejection and solely to expedite allowance of the pending claims, Applicants hereby submit a

terminal disclaimer for the instant application in relation to U.S. Patent No. 6,340,703. With the entry of this Amendment, Response, and Terminal Disclaimer, the double patenting rejection is overcome.

Conclusion

With the entry of this Amendment, claims 1-18, 21, 28-35, and 41-44 are pending. Applicants earnestly and respectfully request the Office to reconsider its assertion of *prima facie* obviousness and to allow the pending amended claims. Should this paper not result in a Notice of Allowance, Applicants respectfully that the Examiner contact the undersigned at 650-849-6677 to arrange for an interview.

If there is any fee due in connection with the filing of this Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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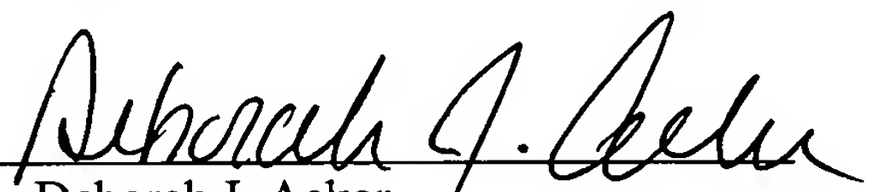
Dated: December 13, 2004

By: 
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